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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/807,993	03/23/2004	James Patrick Dunn	R0169B-REG	4667
24372	7590	06/20/2006	EXAMINER	
ROCHE PALO ALTO LLC PATENT LAW DEPT. M/S A2-250 3431 HILLVIEW AVENUE PALO ALTO, CA 94304			RAO, DEEPAK R	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 06/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/807,993	<b>Applicant(s)</b> DUNN ET AL.	
	<b>Examiner</b> Deepak Rao	<b>Art Unit</b> 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 29 March 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-51 ~~is~~/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-51 ~~is~~/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>062304 &amp; 082604</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Claims 1-51 are pending in this application.

#### ***Election/Restrictions***

Applicant's election without traverse of Group I, drawn to claims 1-51 in the reply filed on March 29, 2006 is acknowledged.

Applicant's election of the species of I-236 is also acknowledged. As the elected species was not found in the prior art, the search was expanded to the elected invention of Group I.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound of formula (I) or an acid addition salt thereof, does not reasonably provide enablement for a **hydrate**, **solvate** or a **clathrate** of a compound of formula (I). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

#### **Factual Basis:**

1. Specification has no working example of hydrate, solvate or clathrate of compound of formula (I); and some of the exemplified compounds within the claimed genus were in contact

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with solvent. Yet they have not formed solvate as evident from spectral data provided for these compounds.

2. Searching the pertinent art in the related pyridazine area did not result in support for such solvates of instant pyridazine compounds. Searching the more general area of solvates resulted in pertinent reference West applied below. West clearly shows lack of predictability of the art in the solvate area.

Based on these two facts, a scope of enablement rejection follows using relevant Wands factors. Hence, the burden of establishing the *prime facie* case is met with.

**Scope of enablement rejection:**

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

**1. The nature of the invention and the state of the prior art:**

The invention is drawn to compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof. Specification is not adequately enabled as to how to make solvate of compounds of formula (I) Specification has no example of hydrate, solvate or clathrate of the instant compounds. Specification on page 22 recites that 'solvate of a compound of formula (I) is a compound that further includes a solvent' but there is no enabling disclosure of such solvates.

The compounds of formula (I) embrace substituted pyridazine compounds substituted with a benzyl group and further substituted on both the pyridazinyl and phenyl rings with various

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substituent groups. Careful calculation of the number of compounds embraced in the instant formula (I) shows a large number of compounds. The term “substituted” (in all occurrences) embraces undefined number of variable groups and thus, the genus embraced by claim 1 is excessively large and there is no teaching of any hydrate, solvate or clathrate of this large genus.

Search in the pertinent art, including water as solvent resulted in a pertinent reference, which is indicative of unpredictability of solvate formation in general. The state of the art is that is not predictable whether solvates will form or what their composition will be. In the language of the physical chemist, a solvate of organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry). The solvent molecule is a species introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West (Solid State Chemistry) says, “it is not usually possible to predict whether solid solutions will form, or if they do form what is the compositional extent”. Thus, in the absence of experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometry of the formed solvate, i.e. if one, two, or a half a molecule of solvent added per molecule of host. Compared with polymorphs, there is an additional degree of freedom to solvates, which means a different solvent or even the moisture of the air that might change the stable region of the solvate. In the instant case of solvate a similar reasoning therefore apply. Water is a solvent and hence it is held that a pertinent detail of West, which relates to solvates, is also applicable to water.

In addition, an additional search resulted in Vippagunta et al., Advanced Drug Delivery Reviews 48: 3-26, 2001, which clearly states that formation of solvates is unpredictable. See entire document especially page 18, right column section 3.4. Note Vippagunta et al., states

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“Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for series of related compounds”.

Joachim Ulrich (Kirk-Othmer Encyclopedia of Chemical Technology) provides that “Pseudopolymorphs are solvates or in the case of water as solvent, hydrates, which means crystals that incorporate solvent molecules into the crystal lattice. Pseudopolymorphs exhibit different crystal forms and/or different densities, solubilities, dissolution rates, colors, hardnesses, etc. Compared with polymorphs, there is an additional degree of freedom (than temperature and pressure), which means a different solvent or even the moisture of the air that might change the stable region of the pseudopolymorph”.

**2. The predictability or lack thereof in the art:**

Hence the solvate as applied to the above-mentioned compounds claimed by the applicant are not art-recognized compounds and hence there should be adequate enabling disclosure in the specification with working example(s).

**3. The amount of direction or guidance present:**

Examples illustrated in the experimental section are limited to making the compounds and not related to solvates or clathrates thereof. There is no example of hydrate, solvate or clathrate of any of the instantly claimed compounds. Many of the exemplified compounds were shown in the specification that have come in contact with water and/or other solvent, however, there is no showing that these compounds formed hydrates, solvates or clathrates. Hence it is clear that merely bringing the compound and water or solvent together does not result in solvate and additional direction or guidance is needed to make them - specification has no such direction or guidance.

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**4. The presence or absence of working examples:**

Determining if any particular substrate would form a solvate, hydrate or clathrate would require synthesis of the substrate and subjecting it to recrystallization with a variety of solvents, temperatures and other parameters. The experimentation is potentially open-ended. The direction concerning the hydrates is found on page 5, which simply states that 'one type of solvate is hydrate', however, there is no working example of any hydrate or solvate formed. The claims are drawn to solvate, yet the numerous examples presented all failed to produce a solvate or even solvate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "[T]he specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there, is no evidence that such compounds exist... the examples of the patent do not produce the postulated compounds... there is ... no evidence that such compounds even exist." The same circumstance appears to be true here. There is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, there should be showing supporting that solvates of these compounds exists and therefore can be made.

**5. The breadth of the claims & the quantity of experimentation needed:**

Specification provides no support, as noted above, for compounds generically embraced in the claim 1 would lead to desired hydrate, solvate or clathrate of the compound of formula (I). As noted above, the genus embraces a large number of compounds and hence the claims are extremely broad. The quantity of experimentation needed would be an undue burden on skilled art in the chemical art since there is inadequate guidance given to the skilled artisan for the many reasons stated above. Even with the undue burden of experimentation, there is no guarantee that

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one would get the product of desired solvate of compound of formula (I) embraced in the instant claims in view of the pertinent reference teachings.

2. Claims 32-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating an HIV-1 infection in a host, does not reasonably provide enablement for treating or **preventing** an HIV infection in a host or treating AIDS or ARC generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that “undue experimentation” would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claims are drawn to ‘a method for **preventing** or treating an HIV infection in a host or treating AIDS or ARC’ and the specification fails to enable one skilled in the art for the recited use. The instant claims appear to be in ‘reach-through’ format. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all diseases, disorders or conditions, for which they lack written



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description and enabling disclosure in the specification. Further, there is no disclosure regarding how the host in need of such activity is identified and how the host is subjected to the treatment HIV infection generally. See MPEP § 2164.03 for enablement requirements in cases directed to structure-specific arts such as the pharmaceutical art.

The scope of the method claims is not adequately enabled solely based on the test assays to measure the inhibition activity in a HIV-1 RT assay provided in the specification in Example 45 at pages 150-151. First, the instant claims cover ‘a method of treating or preventing an HIV infection or treating AIDS or ARC’ generally, which for example, includes conditions caused by HIV-1, HIV-2, etc. that are known to exist and those that may be discovered in the future, for which there is no enablement provided. The use disclosed in the specification is as Non-nucleoside reverse transcriptase inhibitors, useful to treat all types of HIV infections, which include AIDS, etc. Test procedure and assay relied upon at pages 150-151 is drawn to inhibition of HIV-1 reverse transcriptase and results for some of the exemplified compounds are provided in Table 3. There is nothing in the disclosure regarding how this *in vitro* data correlates to the treatment of **all** types of HIV infections or conditions associated with HIV embraced by the instant claims. One of ordinary skill would not know to extrapolate this test data to compounds having the assorted types of substituents provided in the instant claims. The disorders encompassed by the instant claims include AIDS, etc., some of which have been proven to be extremely difficult to treat. There is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure

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for a Markush group.

State of the art references provide that:

- (1) [http://www.hivguidelines.org/public\\_html/center/clinical-education/q-and-a/hiv-2.htm](http://www.hivguidelines.org/public_html/center/clinical-education/q-and-a/hiv-2.htm)

Little is known to date about the effectiveness of current antiretroviral medications against HIV-2 infection, in part, because antiretroviral medications have not been widely available in areas with large numbers of HIV-2 infection. Little is known about whether the current emphasis on early initiation of combination antiretroviral therapy for HIV-1 is appropriate for treatment of HIV-2. Viral load testing, which has become an important tool in treatment planning and monitoring for HIV-1 is not currently available for HIV-2.

- (2) <http://www.aegis.com/aidsline/1992/nov/M92B0027.html>

Calanolides A (1) and B (4) were completely protective against HIV-1 replication and cytopathicity (EC<sub>50</sub> values of 0.1 microM and 0.4 microM, respectively), but were inactive against HIV-2.

Further, the instant claims are directed to 'a method for **preventing** or treating an HIV infection in a host' which is not sufficiently established in the specification. The biological test assays are provided in the specification pages 150-151, however, these assays are directed to determining the *in vitro* anti-HIV activity of the compounds in an HIV-1 reverse transcriptase assay and there is insufficient evidence that such studies correlate with *in vivo* efficacy in treatment of all diseases associated with HIV reverse transcriptases generally, particularly in humans. The obstacles to therapy of HIV are well documented in the literature, which include: 1) the extensive genomic diversity and mutation rate associated with the HIV retrovirus; and 2) the complexity and variation of the pathology of HIV infection in different individuals. HIV-

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specific immunity can control viral replication and delay disease progression but does not clear infection. Antiretroviral treatment consists of inhibitors that target for viral entry, reverse transcriptase, and viral protease. Therapy can control viral replication, restore immunity, and delay disease progression, but it cannot eliminate infection.

Marcus et al. (see the enclosed PubMed Abstract), in their recent publication expressed that 'despite advances, the global spread of HIV and especially its spread in developing countries continues almost unabated'. Also, van Heeswijk et al., (PubMed Abstract enclosed) stated that, "further clinical studies are needed to identify optimal combinations for treatment of antiretroviral naive and experienced HIV-1 infected patients". Despite the unprecedented successes in the therapy of HIV infection, AIDS remains a major world health problem being the first cause of death in Africa and the fourth leading cause of death worldwide. Despite the success of protease and reverse transcriptase inhibitors, new drugs to suppress HIV-1 replication are still needed. Thus it is clear from the above evidence that the ability to treat diseases associated with HIV is highly unpredictable and has met with very little success.

Furthermore, the scope of the claim is not adequately enabled solely based on the assay procedures to measure the HIV-1 RT inhibitory activity provided in the specification. The instant claim is drawn in part to a method of '**prevention** of HIV infection', which is not remotely enabled. The instant compounds are disclosed to have anti-HIV activity and it is recited that the instant compounds are useful in the '**prevention**' of infection by HIV, for which applicants provide no competent evidence. "To prevent" actually means *to anticipate or counter in advance, to keep from happening etc.* (as per Webster's II Dictionary) and therefore it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to

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which the instant compounds can be administered in order to have the “preventive” effect. There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease or disorder claimed herein.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Use of the compounds in treatment as well as **prevention** of HIV infection.

2) The state of the prior art: There are no known compounds of similar structure which have been demonstrated to treat and/or prevent HIV infection generally. The CDC website provides that “At present, no therapy exists to eliminate the human immunodeficiency virus (HIV) or restore an immune system damaged by it. Currently, no vaccine exists to protect susceptible persons from infection.” (see <http://wonder.cdc.gov/wonder/prevguid/p0000072/p0000072.asp>). Further, Miles (2005 Medline abstract enclosed) indicate that “Well into the third decade of the HIV pandemic, there is still no cure on the horizon and recent results of preventive vaccine studies have been disappointing”.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, “the scope of enablement obviously

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varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: There are no doses present to direct one to protect a potential host from the disorders cited, etc. nor there are doses given for the treatment of the disorders recited. The specification provides test procedure to measure the inhibitory activity of the compounds (see pages 150-151) and HIV-1 RT inhibition data for some of the exemplified compounds. However, there is no disclosure regarding how the *in vitro* results correlate to treatment as well as **prevention** of all types of diseases due to infection by HIV.

6) The breadth of the claims: The instant claims embrace treating or **preventing** all diseases associated with HIV infection.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. In the claims, it is recited that “A compound.... **and** hydrates, solvates, clathrates, **and** acid addition salts thereof”, which is unclear because it is not clear if ‘a compound or a salt thereof’ is claimed **or** ‘a **mixture** of a compound and the salt’ is claimed. Replacing with -- A compound..... ~~and-or an~~ acid addition ~~salts~~ salt thereof -- would overcome the rejection.
2. Claim 41 is an independent claim, however, does not contain the definitions of the variables. The claim recites the variables  $R^1$ - $R^4$ ,  $R^7$  and  $R^8$  “are as defined hereinabove” however, does not refer to any claim. An independent claim must contain all limitations within the claim or should refer to another claim containing the limitations.
3. In claim 41, in step (iii), it is recited that ‘the compound of formula IIb is condensed with a **pyrazine** compound to produce a compound of formula IIIa’ and in step (iv) it is recited that ‘hydrolysing chloropyrazine to a pyridazinone of formula I’ - which steps are confusing. The compounds of formula IIIa and formula I are drawn to a pyridazine compounds and it is not understood how the pyrazine (i.e., 1,4-diazine) is converted to pyridazine (i.e., 1,2-diazine). The specification in pages 15-17, does not provide any explanation or help to clarify these steps. Claims 46, 47 and 51 also recite the term ‘pyrazine’.

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4. Claim 47 recites the limitation "said pyrazine **derivative**" in lines 1-2. There is insufficient antecedent basis for this limitation in claim 41 on which claim 47 is dependent. The term "derivative" includes compounds that are derived from another compound and claim 41 recites 'a pyrazine compound'.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Chintakunta et al. (Eur. J. Med. Chem. 2002). The instant claims read on reference disclosed compounds, see compound 6 in page 341 of the reference.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

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evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 41-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chintakunta et al. (Eur. J. Med. Chem. 2002). The reference teaches a process to prepare a pyridazinyl compound (6) by coupling an aryl compound having a methylchloride substituent (3) with a pyridazine compound. The instantly claimed process involves an aryl compound having a methylbromide substituent in place of the reference compound having methylchloride substituent. It would have been obvious to one having ordinary skill in the art to replace the chloro with a bromo because the skilled artisan would have had the reasonable expectation that any of the halogens would make a good leaving group. One of ordinary skill in the art would have been motivated to prepare the aryl compound having methylbromide because he would have expected the methylbromide aryl compound to react analogously as the reference taught aryl methylchloride compound.

Receipt is acknowledged of the Information Disclosure Statements filed on June 23 and August 26, 2004 and copies are enclosed herewith.




***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
**Deepak Rao**  
**Primary Examiner**  
**Art Unit 1624**

June 12, 2006